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1. 1. **ureaplasma**

Author: Fertilitext

Definition:

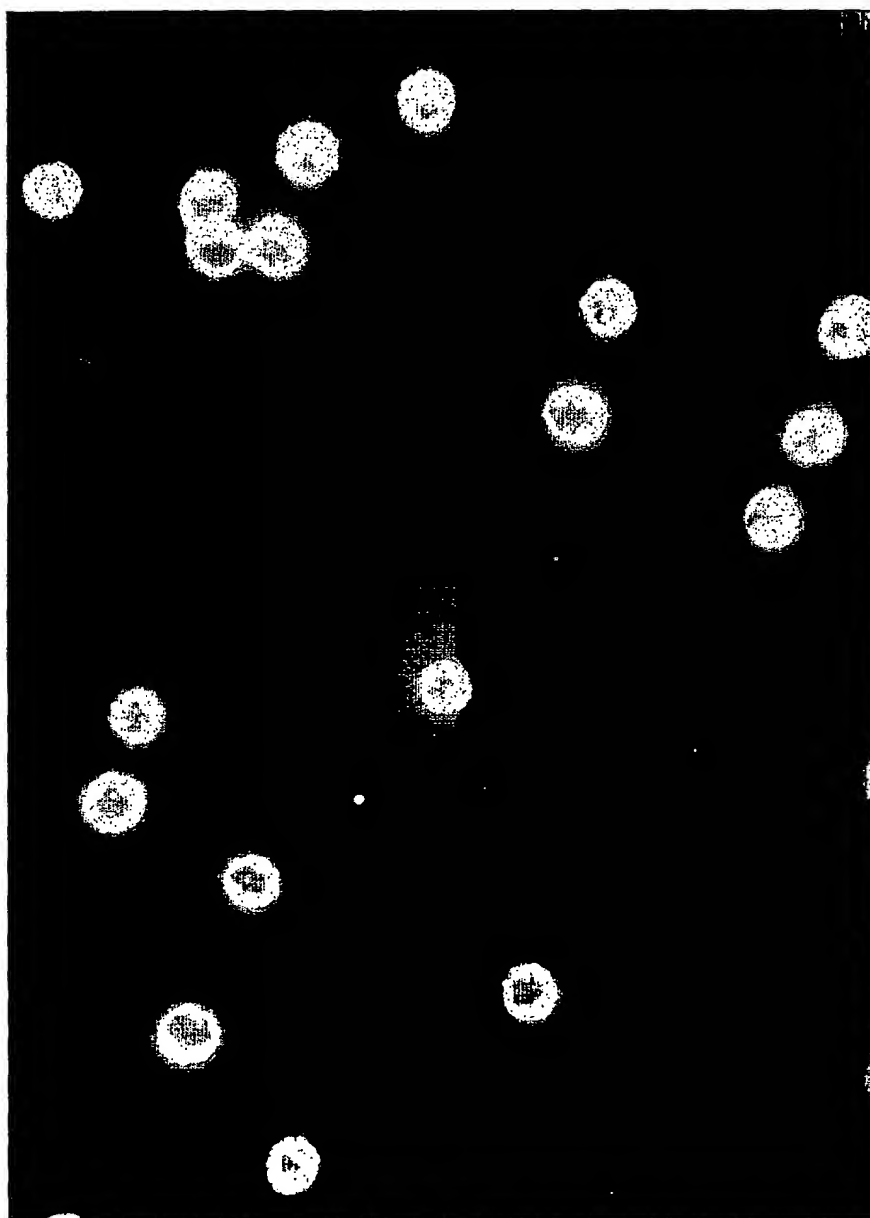
A microorganism that can infect peoples' bladders; ureaplasmas are similar to mycoplasmas.

END

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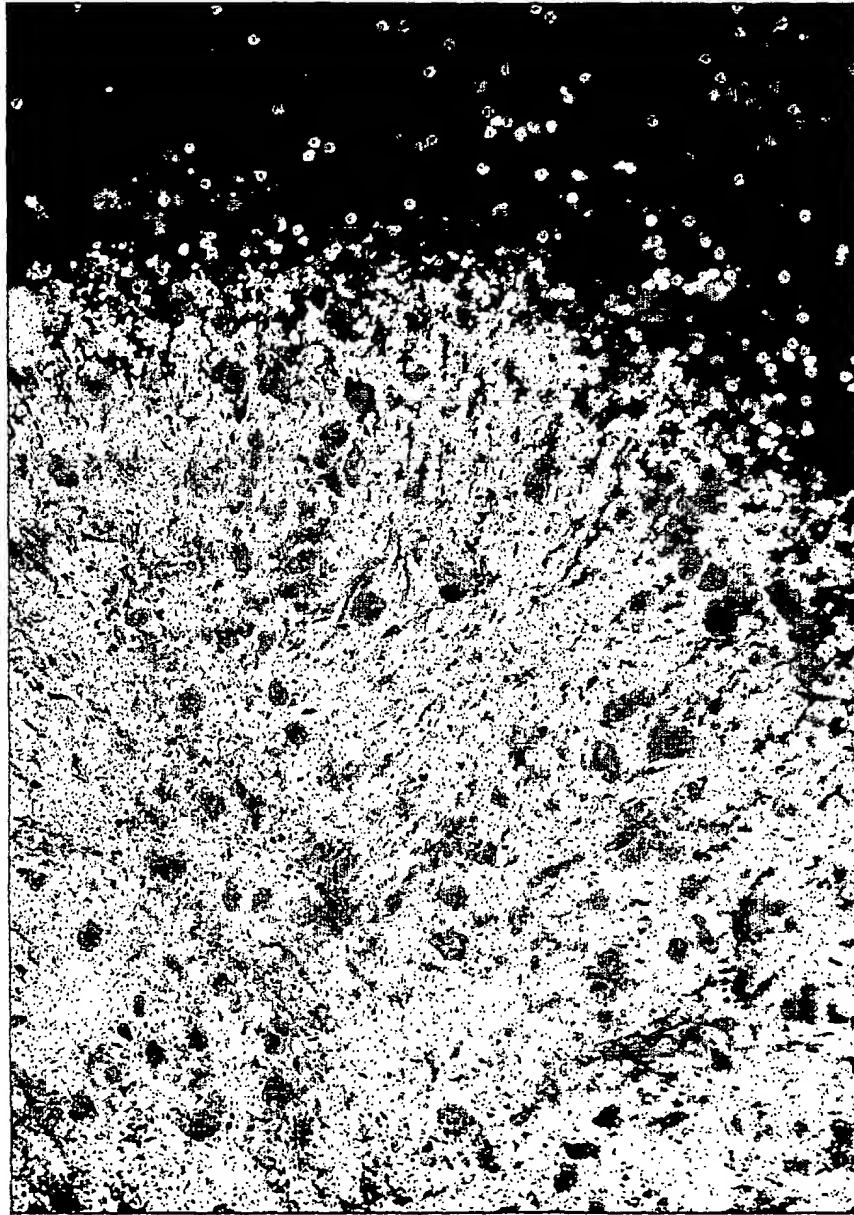
3/4

FIG. 3



4/4

FIG. 4



01395084

NOVEL ORGANISM ASSOCIATED WITH NONGONOCOCCAL URETHRITIS

NOVEL ORGANISM ASSOCIATED WITH NONGONOCOCCAL URETHRITIS

PATENT ASSIGNEE:

Lambl, Barbara B., (3975360), 26 F Sea Breeze Lane, Nahant, MA 01908,
(US), (Applicant designated States: all)

INVENTOR:

Lambl, Barbara B. , 26 F Sea Breeze Lane, Nahant, MA 01908, (US
PATENT (CC, No, Kind, Date):

WO 2001097710 011227

APPLICATION (CC, No, Date): EP 2001941592 010523; WO 2001US16842 010523

PRIORITY (CC, No, Date): US 598604 000621

DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI;
LU; MC; NL; PT; SE; TR

EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI

INTERNATIONAL PATENT CLASS: A61C-019/04; A61B-005/00

LANGUAGE (Publication,Procedural,Application): English; English; English

11661463 PMID: 8974102

A medium chain triglyceride-based diet in patients with HIV and chronic diarrhea reduces diarrhea and malabsorption: a prospective, controlled trial.

Wanke C A; Pleskow D; Degirolami P C; Lambl B B ; Merkel K; Akrabawi S
Division of Infectious Diseases, New England Deaconess Hospital, Boston, Massachusetts 02215, USA.

Nutrition (Burbank, Los Angeles County, Calif.) (UNITED STATES) Nov-Dec 1996, 12 (11-12) p766-71, ISSN 0899-9007 Journal Code: 8802712

Publishing Model Print

Document type: Clinical Trial; Journal Article; Randomized Controlled Trial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS; AIDS/HIV

Our objective was to determine whether a medium-chained triglyceride (MCT)-based diet, compared to a long-chain triglyceride (LCT)-based diet, conveys a beneficial effect on diarrhea and fat malabsorption in human immunodeficiency virus (HIV)-infected individuals with chronic diarrhea and weight loss. A secondary objective was to evaluate the pathogens associated with the diarrhea and to evaluate whether the etiologic agent was a determinant of response to the nutritional intervention. Prospective, randomized double-blind comparative trial was conducted in 24 adult patients with HIV, diarrhea of greater than 4-wk duration, fat malabsorption, and loss of 10-20% of ideal body weight, these patients were recruited from our outpatient infectious disease clinic. Evaluations of diarrheal pathogens were made by complete stool examination, upper and lower endoscopy with quantitative culture, and biopsy. Body composition determinations, and measurements of fat, carbohydrate, and vitamin absorption pre- and postintervention. Patients were randomly assigned to one of two complete nutritional products with either medium- or long-chain triglyceride fat exclusively for 12 d followed by treatment of infectious pathogens. Ten patients were found to have Microsporidium and 9 patients had no identifiable pathogen. All patients responded to intervention with both nutritional products overall with 45% fewer stools, decreased stool fat and weight, and a significant increase in urine nitrogen. The group that received the MCT product demonstrated significantly decreased stool number (mean 4 to 2.5), stool fat (mean 14 to 5.4 g), and stool weight (mean 428 to 262 g) compared with baseline ($P < 0.01$ for all). Patients with both species of microsporidia and with pathogen negative diarrhea had good response. We found that HIV patients with diarrhea, regardless of etiology, and documented fat malabsorption may benefit symptomatically from a diet composed of an MCT-based liquid supplement.

Tags: Male; Research Support, Non-U.S. Gov't

Descriptors: *Diarrhea--diet therapy--DH; *Dietary Fats--administration and dosage--AD; *HIV Infections--complications--CO; *Malabsorption Syndromes--diet therapy--DH; *Triglycerides--administration and dosage--AD ; Adult; Body Mass Index; Diarrhea--etiology--ET; Diarrhea--parasitology--PS; Double-Blind Method; Humans; Malabsorption Syndromes--etiology--ET; Microsporidiosis; Prospective Studies

CAS Registry No.: 0 (Dietary Fats); 0 (Triglycerides)

Record Date Created: 19970317

Record Date Completed: 19970317

8/9/2

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11492334 PMID: 8805864

Malabsorption and wasting in AIDS patients with microsporidia and pathogen-negative diarrhea.

Lamb L B B ; Federman M; Pleskow D; Wanke C A

Division of Infectious Diseases, New England Deaconess Hospital, Boston, MA 02215, USA.

AIDS (London, England) (UNITED STATES) Jun 1996, 10 (7) p739-44,
ISSN 0269-9370 Journal Code: 8710219

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS; AIDS/HIV

OBJECTIVE: To define the clinical syndrome, nutritional status and malabsorptive status in patients with HIV and chronic diarrhea and either microsporidia or no identified pathogen. **PATIENTS:** HIV-positive patients from an urban, hospital-based infectious disease clinic with chronic diarrhea who had undergone exhaustive gastrointestinal and stool studies for enteric pathogens and were found to have either microsporidia or no pathogen. **METHODS:** Patients were evaluated for clinical history, physical, body composition, nutritional and malabsorptive studies including D-xylose, Schilling test, determinations of 24 h stool fat, weight and nitrogen, and 24 h urea nitrogen. **RESULTS:** Ten patients with microsporidia were studied, four of whom were infected with *Septata intestinalis*, six with *Enterocytozoon bieneusi*; nine patients had no identified pathogen. Patients in both groups were comparable in stage of HIV disease, and demonstrated abnormal nutritional status and malabsorptive parameters. Patients with no pathogen had significantly longer duration of symptoms prior to presentation; however, patients with microsporidia had significantly greater malabsorption of fat, D-xylose, vitamin B12, and significantly lower serum levels of zinc. Nutritional status and malabsorption were similarly depressed in patients infected with either species of microsporidia. **CONCLUSION:** HIV-infected patients with chronic diarrhea associated with either microsporidial infection or with no identified pathogen had abnormal parameters of absorption and malnutrition, and those infected with microsporidia demonstrated more severe malabsorption.

Tags: Male; Research Support, Non-U.S. Gov't

Descriptors: *Acquired Immunodeficiency Syndrome--complications--CO;
*Acquired Immunodeficiency Syndrome--metabolism--ME; *Diarrhea--etiology
--ET; *HIV Wasting Syndrome--complications--CO; *HIV Wasting Syndrome
--etiology--ET; *Malabsorption Syndromes--complications--CO; *Malabsorptio
n Syndromes--etiology--ET; *Microsporidia; *Protozoan Infections
--complications--CO; *Protozoan Infections--etiology--ET; Acquired
Immunodeficiency Syndrome--parasitology--PS; Adult; Animals; CD4 Lymphocyte
Count; Dietary Fats--metabolism--ME; HIV Wasting Syndrome--parasitology--PS
; Humans; Malabsorption Syndromes--virology--VI; Protozoan Infections
--metabolism--ME; Vitamin B 12--metabolism--ME; Xylose--metabolism--ME;
Zinc--metabolism--ME

CAS Registry No.: 0 (Dietary Fats); 0 (Xylose); 68-19-9 (Vitamin B
12); 7440-66-6 (Zinc)

Record Date Created: 19970116

Record Date Completed: 19970116

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Malabsorption and wasting in AIDS patients with microsporidia and pathogen-negative diarrhea.

Lambl BB, Federman M, Pleskow D, Wanke CA.

Division of Infectious Diseases, New England Deaconess Hospital, Boston, MA 02215, USA.

OBJECTIVE: To define the clinical syndrome, nutritional status and malabsorptive status in patients with HIV and chronic diarrhea and either microsporidia or no identified pathogen. **PATIENTS:** HIV-positive patients from an urban, hospital-based infectious disease clinic with chronic diarrhea who had undergone exhaustive gastrointestinal and stool studies for enteric pathogens and were found to have either microsporidia or no pathogen. **METHODS:** Patients were evaluated for clinical history, physical, body composition, nutritional and malabsorptive studies including D-xylose, Schilling test, determinations of 24 h stool fat, weight and nitrogen, and 24 h urea nitrogen. **RESULTS:** Ten patients with microsporidia were studied, four of whom were infected with *Septata intestinalis*, six with *Enterocytozoon bieneusi*; nine patients had no identified pathogen. Patients in both groups were comparable in stage of HIV disease, and demonstrated abnormal nutritional status and malabsorptive parameters. Patients with no pathogen had significantly longer duration of symptoms prior to presentation; however, patients with microsporidia had significantly greater malabsorption of fat, D-xylose, vitamin B12, and significantly lower serum levels of zinc. Nutritional status and malabsorption were similarly depressed in patients infected with either species of microsporidia. **CONCLUSION:** HIV-infected patients with chronic diarrhea associated with either microsporidial infection or with no identified pathogen had abnormal parameters of absorption and malnutrition, and those infected with microsporidia demonstrated more severe malabsorption.

PMID: 8805864 [PubMed - indexed for MEDLINE]

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Septata

A recently described member of the protozoan phylum Microspora found in the intestine of an immunocompromised individual. The species described is Septata intestinalis.

(05 Mar 2000)

Previous: [septal gingiva](#), [septal lines](#), [septal nuclei](#), [septan](#), [septane](#), [septangle](#), [septarium](#)

Next: [septate](#), [septate: divided](#), [septate hymen](#), [septate junction](#)

Come to the [European Association for Cancer Education](#) Annual Meeting

Published at the Dept. of Medical Oncology, [University of Newcastle upon Tyne](#)

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Enterocytozoon bieneusi

Agent of microsporidian infection, primarily infecting the small intestine, especially in immunocompromised individuals. It is the microsporidian most frequently reported in AIDS patients, where it has been implicated in chronic diarrhoea and weight loss; suggested treatment has been with octreotide with albendazole.

See: microsporidia.

(05 Mar 2000)

Previous: enterocyst, enterocystocele, enterocystoma, enterocyte, Enterocytozoon
Next: enterodynia, enteroendocrine cells, enteroenterostomy

Come to the European Association for Cancer Education Annual Meeting

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10256159 PMID: 8346204

Composite, large spirochetes from microbial mats: spirochete structure review.

Margulis L; Ashen J B; Sole M; Guerrero R Margulis L U Mass, Amherst, Dept Biology

Department of Biology, University of Massachusetts, Amherst 01003.

Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Aug 1 1993, 90 (15) p6966-70, ISSN 0027-8424
Journal Code: 7505876

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Phenomena previously unknown in free-living spirochetes are reported: large-sized cells with variable diameter (length to 100 microns, width between 0.4 and 3.0 microns), composite structure (smaller spirochetes inside larger ones), and positive phototropic behavior. These bacteria, Spirosymplokos, are compared with all other spirochete genera. The large spirochete, grown in mixed culture, was studied live and by transmission EM. The protoplasmic cylinder was replete with **spherical** granules 20-32 nm in diameter, and three to six periplasmic 26-nm flagella were inserted subterminally. Comparably granulated and flagellated small spirochetes were located inside the protoplasmic cylinder and in the periplasm of the large ones. When exposed to air, movement became erratic, protoplasmic cylinders retracted to lie folded inside the outer **membrane**, and **refractile membranous** structures formed. From one to four structures per still-moving spirochete were seen. Spirosymplokos was enriched from laboratory samples exposed to oxygen-rich and desiccating, but not dry, conditions for at least 4 mo after removal of microbial mat from the field.

Tags: Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, Non-P.H.S.

Descriptors: *Spirochaetales--isolation and purification--IP; Microscopy, Electron; Seawater; Spirochaetales--classification--CL; Spirochaetales--ultrastructure--UL

Identifiers: *NASA Discipline Exobiology; *NASA Discipline Number 52-30; *NASA Program Exobiology; *Non-NASA Center

Record Date Created: 19930907

Pillotina
Crenulation
Sillon
Cytoplasmic
filaments
C. Bistispira

10486289 PMID: 11538110 Record Identifier: 00014783

Cristispira from oyster styles: complex morphology of large symbiotic spirochetes.

Margulis L; Nault L; Sieburth J M Margulis L U MA, Amherst, Botany Dept
Botany Department, University of Massachusetts, Amherst 01003, USA.

Symbiosis (UNITED STATES) 1991, 11 p1-17, ISSN 0334-5114

Journal Code: 9881559

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NASA

Other Citation Owner: NASA

Record type: MEDLINE; Completed

Crystalline styles (digestive organs) of bivalve mollusks provide the habitat for highly motile bacteria. Styles from freshly-collected oysters, *Crassostrea virginica*, were studied by electron microscopy; *Cristispira* spirochetes were abundant in these organs. Detailed study reveals these spirochetes to be among the most complex prokaryotic cells known. More than 600 periplasmic flagella and an adhering outer lipoprotein membrane (e.g., a 270 degrees sillon) form the ultrastructural basis for the "crista," first described by light microscopy. Unique rosette structures corresponding to the "chambers" or "ovoid inclusions" of light microscopy were detected at the periphery of all protoplasmic cylinders. Polar organelles and linearly aligned flagellar insertions are conspicuous. In size and complexity, *Cristispira* more resembles *Pillotina*, *Diplocalyx*, *Clevelandina* and *Hollandina* (large spirochetes symbiotic in termites) than it does *Treponema*. *Cristispira pectinis* (Gross, 1910), the type species; *Spirillum ostrea* (Noguchi, 1921); and another, less frequent bacterial symbiont are the predominant inhabitants of the dense style matrix. The ultrastructure of the spirillum and an electron micrograph of the third bacterium are shown.

Tags: Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, Non-P.H.S.

Descriptors: *Oysters--microbiology--MI; *Spirochaetaceae--ultrastructure--UL; Animals; Flagella--ultrastructure--UL; Microscopy, Electron; Organelles--ultrastructure--UL; Oysters--physiology--PH; Spirochaetaceae--physiology--PH; Symbiosis--physiology--PH

Identifiers: *NASA Discipline Exobiology; *NASA Discipline Number 52-30; *NASA Program Exobiology; *Non-NASA Center

Record Date Created: 19951012

Record Date Completed: 19951012

3210604 PMID: 11334304

Canaleparolina darwiniensis, gen. nov., sp. nov., and other pillotinaceous spirochetes from insects.

Wier A; Ashen J; Margulis L

Department of Geosciences, University of Massachusetts, Amherst 01003-5820, USA. amwier@uwm.edu

International microbiology - the official journal of the Spanish Society for Microbiology (Spain) Dec 2000, 3 (4) p213-23, ISSN 1139-6709

Journal Code: 9816585

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

We describe two new **pillotinaceous** spirochetes (*Canaleparolina darwiniensis*, *Diplocalyx cryptotermittidis*) and identify for the first time *Hollandina pterotermittidis* from both the subterranean termite *Cryptotermes cavifrons* and the wood-eating cockroach *Cryptocercus punctulatus* based on **morphometric** analysis of transmission electron micrographic thin sections. *C. darwiniensis*, gen. nov., sp. nov., limited to near Darwin, Australia, invariably is present on the surface of the treponeme-studded trichomonad *Mixotricha paradoxa*, a consistent inhabitant of the hindgut of healthy termite *Mastotermes darwiniensis*. The spirochete both attached to the surface of protists and free-swimming in the paunch (hindgut) lumen of the insect has 16 periplasmic flagella (16:32:16) and imbricated wall structures that resemble flattened crenulations of **Pillotina**. The flagella surround half the protoplasmic cylinder. *C. darwiniensis* is the largest (0.5 microm diameter x 25 microm length) of the three epibiotic bacteria (two spirochetes, one rod) that comprise the complex cortex of its host *Mixotricha paradoxa*. Several criteria distinguish *Diplocalyx cryptotermittidis* sp. nov. isolated from *Cryptotermes cavifrons* intestine: smaller diameter, fewer flagella, absence of inner and outer coats of the outer membrane, wider angle subtended by its flagella and, most notably, cytoplasmic tubule-associated centers, which are periodic electron dense spheres within the protoplasmic cylinder from which emanate cytoplasmic tubules up to 24 nm in diameter. This is also the first report of abundant populations of *Hollandina* in *Cryptotermes cavifrons* (those populations belong to the species *H. pterotermittidis*). **Morphometric** analysis of the first thin sections of any spirochetes (published nearly 40 years ago by A.V. Grimstone) permits us to identify the large (0.9 microm diameter) free-swimming intestinal symbiont of *Cryptocercus punctulatus* also as *Hollandina pterotermittidis*.

Tags: Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, Non-P.H.S.

Descriptors: *Cockroaches--microbiology--MI; *Isoptera--microbiology--MI; *Spirochaetales--classification--CL; *Spirochaetales--ultrastructure--UL; Animals; Microscopy, Electron--methods--MT

Record Date Created: 20010503

Record Date Completed: 20010927

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Composite, large spirochetes from microbial mats: Spirochete structure review

(round bodies/spirochete membranous bodies/spirochete life history/variable-diameter spirochetes/*Spirosymplokos*)

LYNN MARGULIS*†, JON B. ASHEN*‡, MÓNICA SOLÉ*§, AND RICARDO GUERRERO¶

*Department of Biology, University of Massachusetts, Amherst, MA 01003; and †Department of Microbiology, University of Barcelona, E-08028 Barcelona, Spain

Contributed by Lynn Margulis, March 9, 1993

ABSTRACT Phenomena previously unknown in free-living spirochetes are reported: large-sized cells with variable diameter (length to 100 μm , width between 0.4 and 3.0 μm), composite structure (smaller spirochetes inside larger ones), and positive phototropic behavior. These bacteria, *Spirosymplokos*, are compared with all other spirochete genera. The large spirochete, grown in mixed culture, was studied live and by transmission EM. The protoplasmic cylinder was replete with spherical granules 20–32 nm in diameter, and three to six periplasmic 26-nm flagella were inserted subterminally. Comparably granulated and flagellated small spirochetes were located inside the protoplasmic cylinder and in the periplasm of the large ones. When exposed to air, movement became erratic, protoplasmic cylinders retracted to lie folded inside the outer membrane, and refractile membranous structures formed. From one to four structures per still-moving spirochete were seen. *Spirosymplokos* was enriched from laboratory samples exposed to oxygen-rich and desiccating, but not dry, conditions for at least 4 mo after removal of microbial mat from the field.

Spirochetes, microscopic “wiggly hairs,” were confused with trypanosomes, other protists, and bacteria (1, 2). Although first named by C. S. Ehrenberg in the 1830s, not until ultrastructural studies were undertaken (3, 4) was Noguchi’s claim that spirochetes are bacteria demonstrated unequivocally. A unified group of highly motile prokaryotes, they bear their flagella in the periplasm—i.e., beneath the outer membrane (5). Each helically shaped cell minimally has 2 flagella (e.g., *Spirochaeta*) and maximally >300 [*Cristispira* (6)]. Arranged symmetrically, the flagella tend to overlap. All spirochetes are placed in a single phylum, Spirochaetes (7), of the Kingdom Procaryotae or Monera (8). They are described by the expression $n:2n:n$, where n is the number of flagella at a terminus (Fig. 1). When the flagella are too short to overlap, as in *Leptospira* or *Treponema phagedenis*, the expression becomes $n:0:n$. Sequence analysis of the 16S rRNA confirms the monophyly of all cultivable spirochetes (9). The genera, as determined physiologically and morphologically (10), are correlated with 16S rRNA sequences (9). The five genera of complex symbiotic spirochetes, with crenulations, cytoplasmic tubules, structured coats of the membranes, polar organelles, etc. are not cultivable (11). Morphometrics in uncultivable spirochetes provide the basis for taxonomy (12). Spirochete-cell diameter is usually constant for any strain, whereas physiological conditions that inhibit growth tend to increase cell length. Spirochete diameters vary from 0.09 to at least 3 μm and lengths from 3 to 500 μm . Pathogenic spirochetes associated with syphilis and Lyme disease, respectively, include *Treponema pallidum* ($n = 1$ –3, transmitted sexually) and *Borrelia burgdorferi* ($n =$

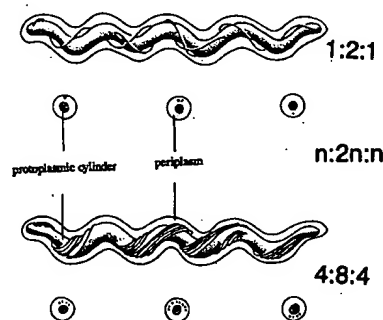


FIG. 1. Spirochete structure showing flagellar arrangement. Drawing was by Christie Lyons.

7–15, borne by ticks, *Ixodes dammini*, *Ixodes pacificus*, *Ixodes ricinus*, and *Ixodes persulcatus*).

Morphometrics of Ehrenberg’s uncultivable “type species” *Spirochaeta plicatilis* (diameter 0.75 μm , ≈ 20 flagella) are unavailable (14). No other “large” spirochetes (>0.5 μm in diameter) are free-living. Except *S. plicatilis*, large spirochetes are in digestive organs of animals—e.g., *Cristispira*, with only a spirillum and a mycoplasma, inhabits the style of molluscs (6, 13). Hindguts of wood-eating cockroaches (*Cryptocercus*) and termites (rhinotermitids, kalotermitids, and hodotermitids) harbor distinctive large spirochetes in great profusion. None have been cultured despite many attempts—e.g., Noguchi (2) and Breznak (13). Placement into anoxic media may prolong survival; yet within hours of removal symbiotic spirochetes die. *T. pallidum* responds to exposure by immediate death (15). Spirochetes reproduce by transverse binary fission. No developmental cycle has been documented for any spirochete.

METHODS AND MATERIALS

Samples were collected from three laminated intertidal microbial mats containing the filamentous cyanobacterium *Mi-*

†To whom reprint requests should be addressed.

‡Present address: Department of Biology, University of California, Santa Cruz, CA 95064.

§Present address: Center for Molecular Biology, Autonomous University of Madrid, E-28049 Canto Blanco, Madrid, Spain.

¶Shocking confusion concerning the identification of spirochetes, especially the causative agent of syphilis (*Treponema pallidum*), persists even among scholars who should be better informed. This recent book exacerbates the problem: “Syphilis has long fed on a hysterical panic that has ill-served the cause of prophylaxis Nowadays, by contrast, syphilis feeds on the carefree disdain of the general public. Can penicillin vanquish it? Of course, but one still has to know that one is contaminated. The *Treponema* is a tiny fragile thing, a vulgar protozoan, not even a virus. But this fragility, which has made it so far impossible to culture *in vitro* and thereby gain a sufficient understanding of its modes of operation, assures its survival!” (boldface type is our emphasis).

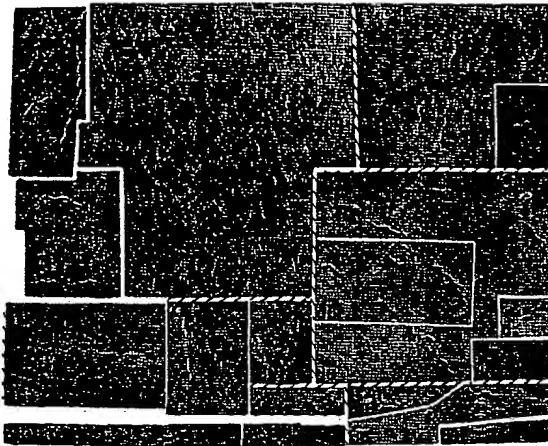


FIG. 2. *Spirosymplokos*, (s) live, with different objectives (p, phase-contrast light micrograph; d, differential interference-contrast micrograph; 4, $\times 140$; 6, $\times 220$; 10, $\times 350$ original magnification). Open arrows, composite structure; solid arrows, round bodies and swellings; arrowheads at m correspond to membranous swellings in Fig. 5 C and D. At double-headed arrow smaller spirochete is attached to larger spirochete. (Bars = 10 μm .)

crocoelus cthonoplastes from Spain (16) and Mexico (figure 1, site 1 in ref. 17 and ref. 18). The best were consistently

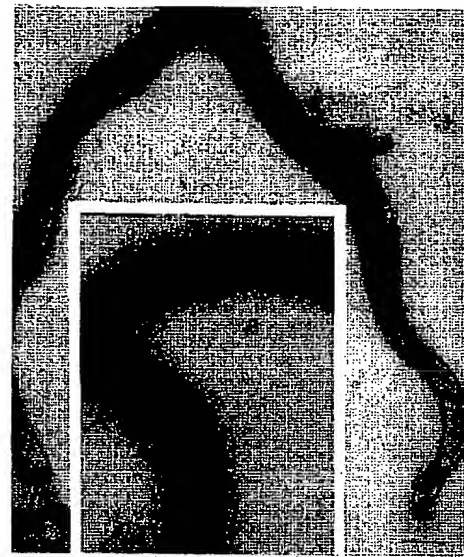


FIG. 3. *Spirosymplokos*, negative stain. (Inset) Higher magnification. g, Granules; f, flagella. (Bars = 1.0 μm .)

obtained at the Alfacs Peninsula of the Ebro delta (16). Enrichments were made by adding 1-cm³ samples of all mat

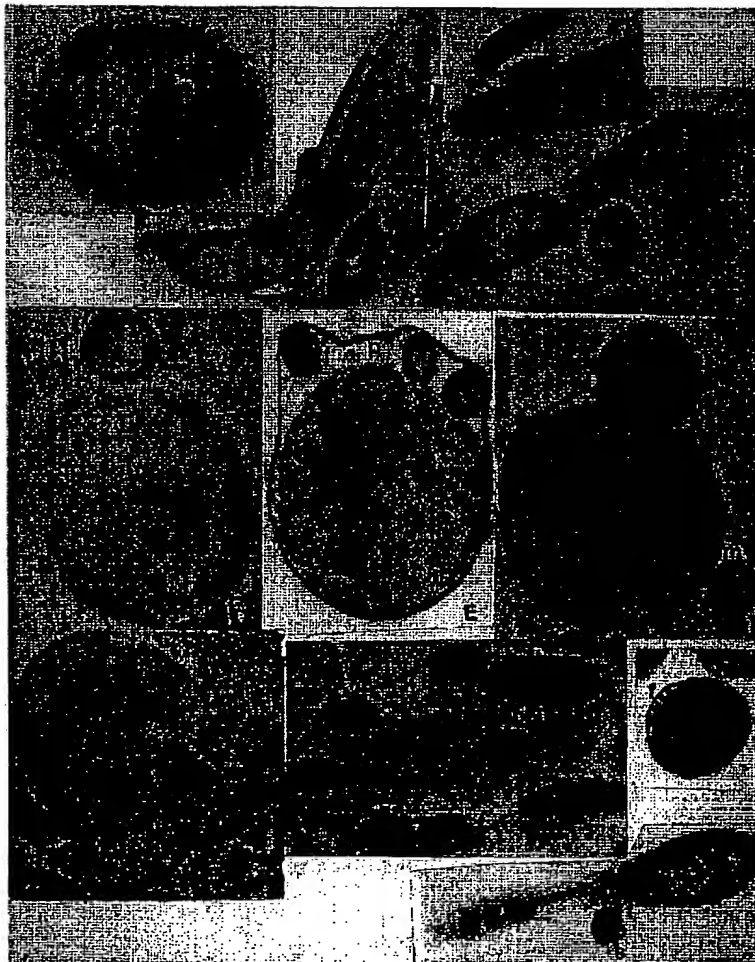


FIG. 4. (A) Composite structure; m, membrane. (B) Cytoplasmic granules may be continuous with components of the periplasmic flagella (f). (C) Formation of new cross walls (cw) inside common periplasm (p). (D) Small granulated spirochete with five flagella (f) in common periplasm of large protoplasmic cylinder. (E) Four protoplasmic cylinders in common periplasm (f, flagella; p, periplasm). (F) Granulated spirochetes both inside and outside outer membrane (m; arrow, cytoplasmic cleavage; f, flagella). (G) Continuity between large and small protoplasmic cylinders (arrow) in transverse section. Smaller spirochete with granulated cytoplasm at right (open arrow). (H) Smaller spirochete (s) apparently emerging (or entering?) through outer membrane (f, flagella). (I) Small spirochete recovered from nearly dry mat material. (J) Smaller diameter spirochete (s) interpreted to be developmentally connected by the flagella (f) to larger one. (K) Small granulated spirochete (cross wall at arrow) attached to the large variable-diameter one.



FIG. 5. (A) Flagella (f) and granules associated with more than a single cylinder, one with its own membrane (m) constricted. Spirochete retracting (or less likely, emerging) at arrows. (B) "Budding-bacteria"-like swellings and development of membranous structures, protoplasmic cylinder cleaved, arrows. (C) Membranous structure (ms) in disintegrating protoplasmic cylinder (pc) in its periplasm (p) probably just before release. (D) Membranous structure (ms, arrow) in small granulated spirochete. (E) Variable diameter (arrow) of large spirochete (f, flagella; c, *Chromatium*-like phototroph). (F) Spirochete membrane (m) thickening.

layers and underlying mud into BA2rif medium (cellobiose/yeast extract/trypticase peptone/antibiotic rifampicin/80% seawater; see refs. 19 and 20 for details). Inoculated tubes were incubated at 22, 25, or 31°C. Spirochete behavior was observed and recorded with a Sony U-Matic videocamera mounted on a Nikon Microphot. Concentrated by centrifugation, spirochetes were prepared for thin section or negative stain transmission EM analysis (5, 12). As detailed (20), samples fixed in 1.25% glutaraldehyde were washed, centrifuged, postfixed in osmium tetroxide, rewashed, dehydrated, and embedded. Stained sections were examined at 80 kV with a JEOL-CS electron microscope.

RESULTS

After inoculation with fresh field samples (6–9 days) in about one-third of the tubes spirochetes "bloomed" (i.e., developed population densities of three to six large spirochetes per field at $\times 400$ magnification). At the height of the bloom, preparations were made for light, video, and EM. Invariably small spirochetes, rods, cocci, and spirilla grew. Sporadically blooms developed of a *Tricercomitus*-like mastigote or the anaerobic ciliate *Trimyxa*.

The large spirochetes were easily seen in phase-contrast at $\times 200$ original magnification (Fig. 2). Only those from Spain were studied in detail. With 1 cm³ of original microbial mat sediment, growth and transfer of the spirochetes was extended for >6 weeks. Boiled, autoclaved, or filtered mud extracts did not suffice. On transfer to fresh BA2rif medium lacking mat, large spirochetes were outgrown by other bacteria. Some small spirochetes were isolated into axenic cultures, and mixed cultures were transferred indefinitely at room temperature or frozen (-80°C or -20°C). Large spirochetes, from seven excursions (August 1990; May and September 1991; February, May, July, and October, 1992), were seen in >40 samples. For at least 4 mo after collection of drying, but still damp, microbial mats placed in jars, spirochetes were grown in anoxic enrichments. Taken from 10

different mat samples, some 250 micrographs of at least 30 different specimens of large spirochetes were analyzed.

The large, loosely coiled spirochete, which swam with both smooth and jerky movements (negatively stained in Fig. 3) consistently had granulated cytoplasm (Figs. 4 and 5). Both uncoordinated and coordinated swimming occurred in the same spirochete: only a portion of the helix moved vigorously or movement occurred in two separated segments of the cell. Single large spirochetes also swam as a unit, for example, when seeking light of the microscopic field. When one end reached the darkened edge of the microscope field closed by an iris diaphragm, the spirochete changed direction moving toward the illuminated center displaying phototaxis (or possibly thermotaxis). Confirmed by videomicroscopy, behaviors were interpreted to be consistent with the composite structure in Figs. 2 and 4 D and G; also refs. 20, 21, and 23.

The ratio of the diameter of the protoplasmic cylinder to the diameter criterion 8 (figure 1C of ref. 12) was larger than any reported; for other morphometrics see ref. 20. From three to six flagella were inserted subterminally at each end. The cytoplasm was replete with dark granules in all protoplasmic cylinders, obscuring any nucleoids. Some of the 26 ± 6 -nm-diameter granules extruded from the cells (ref. 20). The 26-nm-wide flagella were about the same diameter as the granules in >100 micrographs. The granules seemed continuous with the flagella (Fig. 4 A and B). In live and negative-stained cells large spirochete termini were tapered, and yet inside the periplasm of the smaller ones they were blunt (Figs. 3 and 4C), suggesting termini developmentally change as they grow. In each large spirochete, >1 and up to 16 granulated protoplasmic cylinders were present in nearly every transverse, oblique, or longitudinal section (Figs. 4 D–G and 5 A–C). Constant-diameter flagella, associated with both large (3.0 μm) and small (0.4 μm) protoplasmic cylinders were within the same membrane (Figs. 4 C–E, G, J and 5C). Rosettes, cytoplasmic tubules, bundles, and certain other features of large spirochetes were absent (12).

The same spirochete varied in diameter (Figs. 2, 3, 4 G and K, and 5 B and E). Similar small-diameter spirochetes were

found both inside and outside the outer membrane (Fig. 4 D–G, I). Continuity of large with small protoplasmic cylinders and several inside a common membrane is consistent with the idea that the variable-diameter spirochete is composite (Figs. 3, 4 F and G, and 5 B and E). Cross-wall products of cell division and cleaved cytoplasm suggest that small periplasmic spirochetes resulted from multiple fission (Figs. 4G and 5B; also ref. 20 and in ref. 21 figures 9–3 and 9–13). Live small spirochetes seem to be released through the membrane of the large ones. Small spirochetes, from one to three per cell, were seen attached to, perhaps emerging from (or entering?), large swimming ones, comparable to the micrographs of Figs. 2; 4 F, H, and K; and 5 C and E. That different-diameter spirochetes contained fully granulated cytoplasm (Figs. 4 and 5) and connections exist between the flagella of smaller and larger diameter spirochetes (Fig. 4J) support the idea that smaller spirochetes came from composite larger ones.

The large spirochetes became swollen on exposure to air (Fig. 2, Fig. 5 B and E). Some were videotaped as they actively withdrew their protoplasmic cylinders into the periplasm, a process captured in light (Fig. 2, solid arrows) and by EM (Fig. 5A). The onset of erratic, slower swimming, swelling, and withdrawal appeared developmental. Within a few hours while they continued to move, from one to four refractile bodies formed in nearly all. These became visible after the protoplasmic cylinders were withdrawn (m in Fig. 2). Refractile bodies prominent in swollen live spirochetes (Fig. 2, ref. 20) correspond to membranous structures in electron micrographs of Figs. 5 C and D and in ref. 20. Such behavior was not seen in desiccating cultures of *Spirochaeta* (*S. littoralis* or *Spirochaeta* sp. DE-1, refs. 19 and 23).

At all three sites in >20 trials [Spain (16), Laguna Figueroa (17), and Guerrero Negro, Mexico (18)] the spirochetes came only from laminated *Microcoleus* mats. Granulated-cytoplasm spirochetes were in contact with *Chromatium*-like cells in thin sections, suggesting they feed on photosynthate. Large spirochetes not yet studied were enriched from mats at

Santa Pola (Alicante, Spain), Tenerife (Canary Islands, Spain), and Sippewissett salt marsh (Massachusetts) in which the phototroph *Microcoleus chthonoplastes* was underlain by purple sulfur bacteria (*Thiocapsa* sp., *Chromatium* sp., and others). Damp mats were adequate but large composite spirochetes were not retrieved from entirely dry samples.

DISCUSSION

The morphometric description led us to introduce into the literature the Ebro delta large microbial mat spirochete as *Spirosymplokos deltaeiberi* (20). The generic name meaning braid or complex helix refers to composite morphology, the specific to where it was first found. It is compared with all 12 other spirochete genera in Table 1. An analytical drawing based on EM depicts *Spirosymplokos* with the other seven showing complex ultrastructure (Fig. 6). Only *Spirosymplokos* large spirochetes do not inhabit animal digestive organs.

Spirosymplokos by hypothesis undergoes morphogenesis: protoplasmic cylinder cleaves forming smaller spirochetes released from the parent. In response to air (oxygen, desiccation?) refractile bodies develop. Both the smaller and the larger protoplasmic cylinders (Figs. 4 D, E, G, H, and 5A) may provide source material for flagellar development. The paucity of flagella in the large cell raises questions: can so few flagella generate such active motility or might granules con-

Table 1. Comparison of morphology of all spirochete genera

Genus*	Habitat, characteristics	Number of flagella, range	Diameter, μ m range and refs. for distinctive features†
<i>Borrelia</i>	Ticks, +, an, mi	7–15	0.2–0.5 (22)
<i>Clevelandina</i>	Termites, –, an	30–45	0.4–0.8 (11, 12)
<i>Cristispira</i>	Styles of bivalve molluscs; –, mi	100–300	0.5–3.0 (6, 13)
<i>Diplocalyx</i>	Termites, –, an	40–60	0.7–0.9 (11, 12)
<i>Hollandina</i>	Wood-eating cockroaches, termites, –, an	30–60	0.4–1.0 (11, 12)
<i>Leptonema</i>	Vertebrates, +, ac	1–4	0.1–0.3 (10, 24)
<i>Leptospira</i>	Vertebrates, +, ac, free-living	1–4	0.1–0.3 (10, 24)
<i>Mobilifilum</i>	Microbial mats, –, an	10	0.25 (25)
<i>Pillotina</i>	Termites, –, an	40–80	0.6–1.5 (11, 12)
<i>Serpulina</i>	Vertebrates, +, an	8–9	0.1–0.4 (9, 25)
<i>Spirochaeta</i>	Mud, +, an, mi, facultatively an	1–20	0.2–0.75 (14)
<i>Treponema</i>	Vertebrates, +, an	1–16	0.09–0.7 (5, 10, 26)
<i>Spirosymplokos</i>	Microbial mats	3–6	0.4–3.0 (20, 23, this paper)

*Transmission EMs of transverse sections and drawings based on these and many others are depicted in Fig. 6; Figs. 4 and 5 show distinctive morphology of *Spirosymplokos*. +, Some cultivable; –, uncultivable; ac, aerobic; an, anaerobic; mi, microaerophilic. Table was constructed from refs. 5, 6, 10–14, 20, and 22–27.

†Distinctive features are as follows: Lyme disease agent (*Borrelia*); chambered inner coat of outer membrane, sillon (*Clevelandina*); rosettes, flagellar bundle (*Cristispira*); thick outer coat of inner membrane, cytoplasmic tubules (*Diplocalyx*); developed outer coat of outer membrane usual, cytoplasmic tubules, polar organelle (*Hollandina*); cytoplasmic tubules, bent ends, gram + type basal flagella complex (*Leptonema*); leptospiriosis agent (*Leptospira*); double outer membrane, polar organelle, flagellar bundle (*Mobilifilum*); crenulations, sillon, cytoplasmic tubules (*Pillotina*); swine-dysentery agent (*Serpulina*); vast group free-living: marine, freshwater, soil (*Spirochaeta*); syphilis, yaws agents (*Treponema*); composite protoplasmic cylinders, granulated cytoplasm, membranous bodies (*Spirosymplokos*).

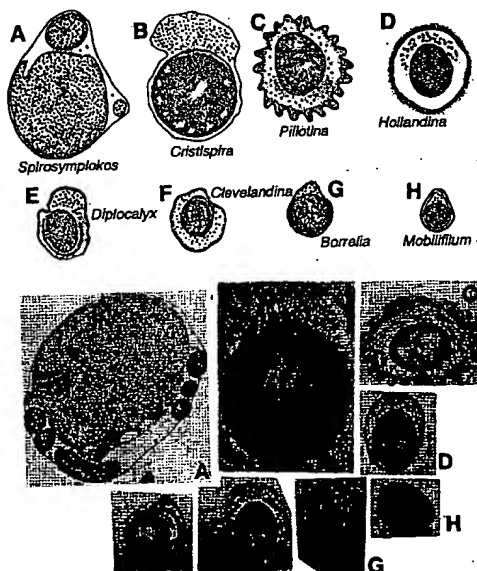


FIG. 6. Eight genera of complex spirochetes. Drawing by C. Lyons was based on text and Table 1. Transverse sections of eight genera are ordered by diameter size. *Cristispira* are from molluscs, and *Borrelia* are from mammals and ticks; other symbionts occur in isopteran digestive systems. Microbial mat *Spirosymplokos* and *Mobilifilum* only are free-living.

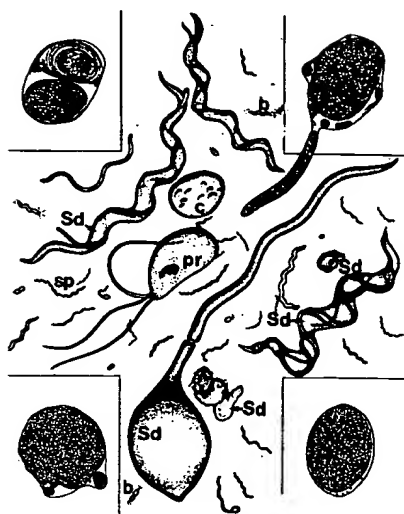


FIG. 7. *Spirosymplokos deltaeiberi* (Sd) reconstructed from live material and from micrographs as in corners of drawing. Variable-diameter large composite spirochetes release small ones. Swollen protoplasmic cylinders withdraw before formation of hypothetically viable membranous bodies. Members of community include *Chromatium* (c), anaerobic protists (pr), small spirochetes (s), and other bacteria (b). Drawing was by C. Lyons.

tain motility proteins? Of the spirochetes only *Cristispira* (6) has some granulated cytoplasm. Granules strewn on grids in negative-stained preparations (shown in refs. 20 and 23) are not fixation artifacts; whether these are related to flagellar components or to ribosomes (they are larger than typical 20-nm ribosomes) is unresolved. As membrane segregates growing cylinders (Figs. 4 F, G, and 5B), granule proteins may contribute to newly forming distally assembling flagella. Swellings (Fig. 2) correlated with the "budding-bacteria"-like appearance (Figs. 5 B and E) precede refractile body formation. The hypothetical developmental scheme as interpreted from life, videotape, micrographs of Figs. 4 and 5, and many not shown, is in Fig. 7. Cytoplasm in predatory prokaryotes differs from that of prey (28), and our micrographs were of vigorously growing cultures; the idea that small spirochetes inside parasitize the larger one is implausible.

The refractile, membranous bodies provide a morphological basis for possible oxygen and desiccation resistance. The transformations may relate (i) enrichability of spirochetes from desiccating microbial mats, (ii) the formation of spirochete round bodies, and (iii) the unpredictable appearance of spirochetes in tissues of syphilis and Lyme disease patients. Chronic spirochetoses symptoms and correlated motile bacteria often reappear after long dormancy periods (1). Although the explanation must also be immunological, the possibility must be reconsidered that symptom reappearance is related to spirochete differentiation; in culture round bodies may be abortive development stages (29).

Anoxygenic and oxygenic phototrophic bacterial mats are one of the oldest ecosystems on Earth. Mud spirochetes, aerotolerant anaerobic chemoheterotrophs that survive changing intertidal environments, are probably among the most ancient mat inhabitants. Ancestors of the large intestinal spirochetes most likely were mud-dwellers originally ingested with algal debris. That the rigors of littoral environments can be tolerated is consistent with an ancient history and early diversification of resistant spirochetes. Morphogen-

etic transformation in these fast-moving bacteria can be used as another argument that, in eukaryosis, undulipodia (cilia, sperm tails) evolved from spirochetes. Free-living spirochetes capable of responsive morphogenesis were the hypothetical ancestors of the now-intracellular microtubule/centriole-kinetosome system. The likely way in which, as motility symbionts, spirochetes literally insinuated themselves into *Thermoplasma* to become the eukaryotic cell lineage is detailed in ref. 21.

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Cyclospora species as a gastrointestinal pathogen in immunocompetent hosts.

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Previous reports of diarrhea resulting from Cyclospora species have been linked to travelers and immunocompromised patients. We conducted a prospective study of 1,042 formalin-ethyl acetate fecal concentrates collected from patients with diarrhea. Between May and November 1993, we identified three patients for whom studies were positive for nonrefractile **spherical** organisms measuring 10 microns in diameter and containing a cluster of **refractile membrane**-bound globules. The cysts exhibited variable acid fastness consistent with Cyclospora species. These three patients had no history of recent travel and presented with relapsing, watery, nonbloody diarrhea that lasted from 12 days to 8 weeks. No other parasitic or bacterial pathogens were identified in their stools. All three instances of diarrhea occurred in May or June. No common source of food or water was identified. None of these patients were immunosuppressed, and their diarrhea resolved spontaneously. We suggest that Cyclospora species should be considered in community-acquired diarrhea.

Tags: Female; Male

Descriptors: *Coccidiosis--etiology--ET; *Diarrhea--etiology--ET; *Eucoccidiida--pathogenicity--PY; Adult; Animals; Coccidiosis--parasitology--PS; Community-Acquired Infections--etiology--ET; Community-Acquired Infections--parasitology--PS; Diarrhea--parasitology--PS; Eucoccidiida--isolation and purification--IP; Feces--parasitology--PS; Humans; Immunocompetence; Middle Aged; Prospective Studies

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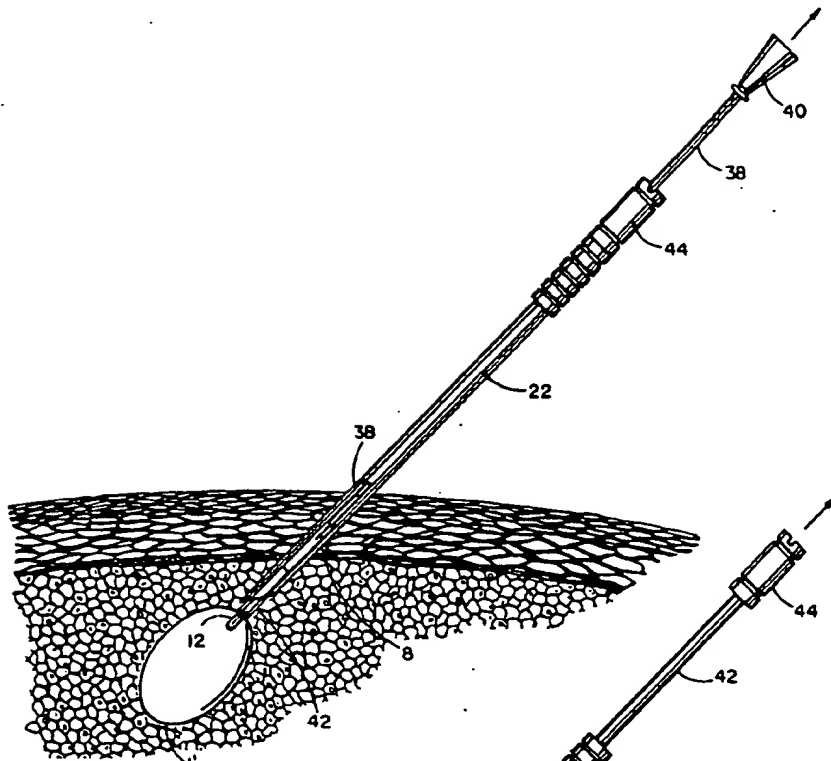


FIG. 10

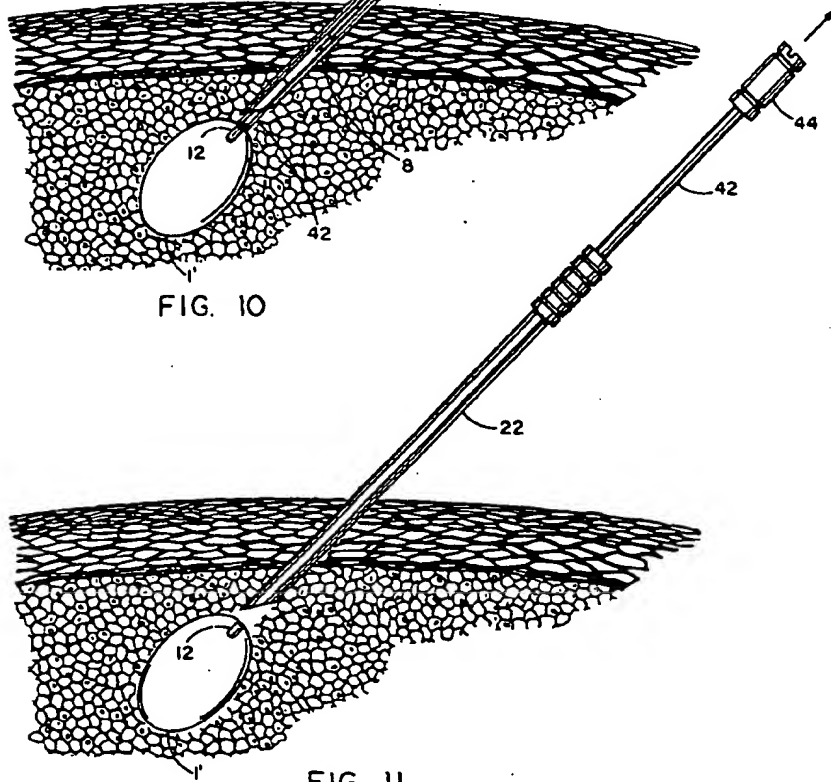


FIG. 11

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Jun 23, 1998

US-PAT-NO: 5769813

DOCUMENT-IDENTIFIER: US 5769813 A

TITLE: Indicator tampon applicator

DATE-ISSUED: June 23, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Peiler; Frances K.	Kaneohe	HI	96744	N/A
Peiler; Larisa H.	Stamford	CT	06902	N/A

US-CL-CURRENT: 604/11; 604/285

CLAIMS:

The invention claimed is:

1. A tampon applicator comprising;
a housing member capable of holding an insertable member;
said housing member supporting at least one pH indicator, wherein
said pH indicator would come into direct contact with a body fluid upon insertion
of the applicator into an individual and provide an instant pH reading upon
removal of the applicator.

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Chlamydia (kla-mid'ē-ă)

The only genus of the family Chlamydiaceae, including all the agents of the psittacosis-lymphogranuloma-trachoma disease groups; chlamydia are obligatory intracellular spherical or ovoid bacteria with a complex intracellular life cycle; the infective form is the elementary body, which penetrates the host cell, replicating as the reticulate body by binary fission; replication occurs in a vacuole called the inclusion body; chlamydia lack peptidoglycan in their cell walls; the type species is *Chlamydia trachomatis*. Formerly called *Betsonia*.
Syn: Chlamydozoon

[G. *chlamys*, cloak]

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